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November 1, 2005

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket No. 2005N-0345

Dear Madam or Sir:

We submit these comments on behalf of Aventis Pharmaceuticals Inc. and Sanofi-Synthelabo Inc., members of the sanofi-aventis Group, in response to the advanced notice of proposed rulemaking published by the Food and Drug Administration ("FDA" or "Agency") on September 1, 2005, regarding the circumstances under which an active ingredient may simultaneously be marketed in both a prescription and an over-the-counter ("OTC") drug product.[1] The sanofi-aventis Group is the world's third largest pharmaceutical company. The sanofi-aventis Group is a dynamic organization that is working to meet the healthcare needs of physicians and their patients and is committed to researching, developing and bringing to market new and innovative healthcare products.

In its September 1, 2005 Federal Register notice, FDA solicited comments as to whether it should commence rulemaking to codify its interpretation of section 503(b) of the Federal Food, Drug, and Cosmetic Act ("FDCA" or "the Act") regarding when an active ingredient can be marketed as both a prescription and OTC drug product.[2] Specifically, FDA requested comments on whether there is "significant confusion regarding FDA's interpretation" of section 503(b) and if so, whether a rulemaking on the issue would resolve the confusion.[3]

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1 70 Fed. Reg. 52050 (Sept. 1, 2005).

2 *Id.* at 52050-51.

3 *Id.* at 52051.

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FDA has consistently interpreted section 503(b)(1) as permitting the marketing of the same active ingredient in products that are both prescription and OTC only if there is "some meaningful difference" between the two, for example in conditions of use, strength, route of administration, or dosage form.[4] FDA has never permitted the same active ingredient to be marketed simultaneously as both a prescription and OTC product for identical conditions of use.

Nevertheless, sanofi-aventis believes that there is indeed significant confusion over the Agency's interpretation of section 503(b) — confusion created by the Agency's October 1999 Draft Guidance for Industry regarding "Applications Covered by Section 505(b)(2)."[5] However, sanofi-aventis believes that FDA need not initiate rulemaking to dispel this confusion. Rather, the Agency can simply withdraw or amend its 1999 Draft Guidance. In addition to noted confusion, the Draft Guidance raises issues of the Agency's unauthorized "taking" of confidential data belonging to the pioneer manufacturer and the Agency's authority under section 505(b)(2), which are beyond the scope of these comments.

An application under section 505(b)(2) of the FDCA is one for which the investigations of safety and effectiveness on which the applicant relies for approval "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use . . . ."[6] In its 1999 Draft Guidance, FDA advanced for the first time its unsupported interpretation of section 505(b)(2) as permitting reliance on proprietary data contained in another manufacturer's application. FDA also asserted in the Draft Guidance that a section 505(b)(2) application could be used to obtain a switch in product indications from prescription only to OTC.[7]

Insofar as it suggested that a section 505(b)(2) application is a suitable vehicle for obtaining approval of a switch from a prescription indication to an OTC indication *for another applicant holder's product,* the Agency's Draft Guidance does not account for the potential for Durham-Humphrey misbranding issues. Under the Draft Guidance, the Agency could theoretically approve an OTC product in reliance on a pioneer's data for an approved prescription product. That prescription product would continue to be covered by the pioneer's NDA. The pioneer with an approved NDA for its product is entitled to – indeed

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4 *Id.*

5 FDA, *Draft Guidance for Industry: Applications Covered by Section 505(b)(2)* (October 1999) (hereinafter "1999 Draft Guidance" or "Draft Guidance").

6 FDCA § 505(b)(2), 21 U.S.C. § 355(b)(2).

7 1999 Draft Guidance at 5.

must – sell that product in conformity with the terms of its NDA, including selling it only as a prescription product. Through its Draft Guidance, the Agency thus opened the door to the same active ingredient being simultaneously marketed for the same conditions of use as both a prescription and an OTC drug product, thereby creating an unworkable tension with section 503(b) of the FDCA.

Significantly, any attempt to remedy the inherent confusion of the Agency's Draft Guidance by forcing the innovator company to take its product OTC upon approval of another applicant's section 505(b)(2) application would raise serious legal concerns. Among other things, section 503(b) of the FDCA does not anticipate such broad-based OTC switches absent rulemaking.[8] In addition, questions of constitutional rights must be addressed.

FDA need not initiate rulemaking to clarify its interpretation of section 503(b) of the FDCA as to when the same active ingredient may be simultaneously marketed in both a prescription and OTC product. Rather, the Agency can do so simply by withdrawing or amending its 1999 Draft Guidance. By withdrawing that guidance or striking any reference to OTC switches in that document, FDA will affirm its practice (1) of permitting switches through the original applicant's initiative or the Agency's own rulemaking and (2) of allowing the same active ingredient to be marketed simultaneously as a prescription and OTC counter product only where a meaningful distinction between the two products exists.

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Sanofi-aventis appreciates the opportunity to comment on this advanced notice of proposed rulemaking.

Sincerely,

Peter O. Safir
Kelly A. Falconer

Counsel for Aventis Pharmaceuticals Inc. and Sanofi-Synthelabo Inc., members of the sanofi-aventis Group

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8 FDCA § 503(b)(3); 21 U.S.C. § 353(b)(3).